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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/061,201	01/30/2002	Mark Shannon	PB0178	2093

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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/061,201	SHANNON, MARK	
	Examiner	Art Unit	
	Jon Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *7,13-31,34-38 and 40-47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-12,32,33 and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *30 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 2/28/05. The amendment filed 2/28/05 is acknowledged. The amendment has been entered. Claims 1-47 are currently pending in the application and are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Election/Restrictions

This application contains claims 7, 13-31, 34-38 and 40-47 drawn to an invention nonelected with traverse in the paper mailed 7/1/04. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-6, 8-12, 32, 33 and 39 are examined herein.

Specification and Sequence Compliance Objection

The Objections based on the presence of hyperlinks in the specification and for sequence compliance issues has been withdrawn in view of the amendment submitted 2/28/05.

Claim Rejections - 35 USC § 101/112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8-12, 32, 33 and 39 are finally rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or, alternatively, a well-established utility, as previously indicated in the paper mailed 10/0/04 and provided below for convenience.

The pending claims have been reviewed in light of the Revised Interim Utility Examination Guidelines and the Revised Interim Written Description Guidelines Training Materials.

The examiner is using the following definitions in evaluating the claims for utility.

"Credible" - Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record that is probative of the applicant's assertions. That is, the assertion is an inherently unbelievable undertaking or involves implausible scientific principles.

"Specific" - A utility that is *specific* to the subject matter claimed. This contrasts with a *general* utility that would be applicable to the broad class of the invention.

"Substantial" - A utility that defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

"Well-established" - a specific, substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art.

The instant claims are drawn to an isolated nucleic acid that encodes a POSH-like oncoprotein (POSHL1), including degenerate variants thereof, probes specific for said nucleic acid, a vector comprising said nucleic acid, a host cell transformed with said nucleic acid, and compositions comprising said nucleic acid wherein said compositions are designated "diagnostic" and "pharmaceutical" compositions. Since all claims encompass, to some extent, an isolated nucleic acid encoding a POSH-like oncoprotein, the utility for all claims require that the isolated nucleic acid encoding the POSH-like protein has utility. With respect to the probes, since the probes are only disclosed as useful for hybridizing to (and thus identifying in a sample) a nucleic acid encoding POSH-like protein, the nucleic acid encoding the POSH-like must have utility in order for the claimed probe to have utility.

Looking to the specification for an assertion of a credible, specific and substantial utility, for the claimed invention, it is noted that the specification asserts the following about the claimed isolated nucleic acids:

> "[T]he present inventors have identified human POSHL1, a proto-oncogene/oncogene product that functions as an adaptor protein that interacts with Rho family small GTpases as well as downstream components of the signal transduction pathway...
>
> [T]he newly isolated gene product shares certain protein domains and an overall structural organization with mouse POSH protein. **The shared structural features strongly imply that human POSHL1 plays a role similar to that of mouse POSH protein** in interacting with members of the Rho family small GTpases, as well as components of the JNK kinase cascade. **POSHL1 is a potential proto-oncogene/oncogene**...

> Like mouse POSH protein, human POSHL1 has one N-terminal RING finger domain and several SH3 domains (three SH3 domains for POSHL1 and four for POSH)... E3 ubiquitin-protein ligase activity is intrinsic to the RING finger domain of c-cbl and is likely to be a general function of this domain. Various RING finger domains exhibit binding activity towards E2 ubiquitin-conjugating enzymes (Ubc' s). SH3 (Src homology 3) domains are often indicative of a protein involved in signal transduction related to cytoskeletal organization. SH3 domain was first described in the Src cytoplasmic tyrosine kinase. The structure of SH3 is a partly opened beta barrel."
>
> (See page 6, line 6 through page 7, line 2 of the specification, emphasis added).

Therefore, applicants have asserted that the claimed invention has utility because human POSHL1 is a proto-oncogene/oncogene product that functions as an adaptor protein that interacts with Rho family small GTpases as well as downstream components of the signal transduction pathway. This is accepted as a credible utility.

However, with respect to the asserted utility as it applies to a specific and substantial utility, it is noted that there are many proto-oncogenes/oncogenes that are known in the prior art. However, the known genus of proto-oncogenes/oncogenes encompass molecules that are structurally and functionally different. Considering that proto-oncogenes/oncogenes encompass a genus of molecules that have different chemical structures (i.e., different sequences) that function by different mechanisms to cause oncogenesis (e.g., they may utilize different signal transduction pathways), it is required that the activity that is specific for POSHL1 be disclosed. Since applicants have merely asserted that the claimed invention has utility as a proto-oncogene/oncogene without asserting any activity that is specific for POSHL1, the asserted utility is not a specific utility. It is noted, that the specification has based the asserted utility on the basis of the sequence homology of human POSHL1 with mouse POSH. The sequence homology analysis indicates that human POSHL1 may contain some of the domains that are

present in mouse POSH. However, it is clear that the human POSHL1 and mouse POSH do not comprise identical domain structure (i.e., they differ in number of certain domains). Furthermore, the specification discloses that POSHL1 functions as an adaptor protein that interacts with Rho family small GTpases as well as downstream components of the signal transduction pathway. However, it is noted that are many different types of GTPases known in the prior art, including GTPases which have divergent functions in the cell. Additionally, the specification discloses that POSHL1 interacts with "downstream components of the signal transduction pathway". It is noted that there are thousands of different signal transduction pathways known in the cells, including pathways that use different downstream components, yet the specification has not identified which downstream components of which signal transduction pathway specifically interacts with POSHL1. That is, there is no data presented which indicates that POSHL1 specifically interacts with any specific GTPase or any specific downstream component of a signal transduction pathway. All of the asserted utilities are based solely on the sequence similarity of human POSHL1 to mouse POSH. It is also noted that the specification acknowledges that the actual function of human POSHL1 has not been determined by stating, "The shared structural features strongly imply that human POSHL1 plays a role similar to that of mouse POSH protein in interacting with members of the Rho family small GTpases, as well as components of the JNK kinase cascade. POSHL1 is a potential proto-oncogene/oncogene..." (See p. 6, lines 12-19).

As indicated above, a substantial utility is one that has "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities. In the instant case, there is no "real world"

utility for the claimed invention because additional experimentation is required in order to first establish that human POSHL1 interacts with specific Rho GTPases and specific downstream components of the signal transduction pathway such that the function of POSHL1 in oncogenesis was clear. Furthermore, there are no asserted utilities found in the specification that would constitute a "real world" use for human POSHL1 without performing additional experimentation. As such, the claimed invention does not have substantial utility.

The last consideration is whether or not the there is a well-established utility that is specific, substantial and credible. A well-established utility may be found in the prior art, the specification or may be readily apparent to one of skill in the art. In the instant case, there is no well-established utility that is credible, specific and substantial found for the claimed isolated nucleic acid(s) encoding a POSH-like protein.

Additionally, claims 1-6, 8-12, 32, 33 and 39 are also finally rejected under 35 U.S.C. 112, first paragraph because, as indicated in the paper mailed 10/20/04: since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

In addition to the 101 rejection above, claims 1-6, 8-12, 32, 33 and 39 are finally rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant rejection is set forth with respect the claims encompassing nucleic acids encoding a polypeptide "at least 90% identical in sequence to SEQ ID NO: 3" (e.g., see claim 1, part (b)(ii)). **It is noted that claim 1 has been amended to include the limitation "at least 90% identical in sequence to SEQ ID NO: 3", thus necessitating this rejection.**

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Thus, an applicant complies with the written-description requirement by describing the invention, with all its claimed limitations, and by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical, structure/function correlation, methods of making the claimed product, and any combination thereof.

The instant claims encompass a genus of nucleic acid molecules that encode polypeptides that are at least 90% identical to SEQ ID NO: 3 wherein the polypeptides can comprise

mutations including deletions, substitutions and/or additional amino acids. Therefore, the claims encompass possibly millions of different variants considering every possible molecule encompassed by the claims. Additionally the claimed genus encompasses molecules which can have completely different function than the polypeptide of SEQ ID NO:3, and possibly including non-functional mutants of SEQ ID NO: 3 which are 90% identical to SEQ ID NO: 3.

It would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of the biomolecule in many instances, albeit not in all cases. In the absence of factual evidence characterizing the structural and functional components of the biomolecule, the effects of these changes are largely unpredictable as to which ones will have a significant effect and which ones will be silent mutations having no effect. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Attwood (Science, 290:471-473, 2000; previously cited); Russell et al. (Journal of Molecular Biology, 244:332-350, 1994; previously cited). However, this level of factual evidence is absent here. Considering that the claims encompass thousands, if not millions of different polypeptides, additional experimentation would be required to determine

which variants encompassed by the claims are functional variants and if the functional variants have identical function to POSHL1 (SEQ ID NO: 3).

Response to Arguments

Applicant's arguments filed 2/28/05 have been fully considered but they are not persuasive.

Applicant points out that claimed subject matter comprises nucleotide sequences encoding a human POSH like protein, which is homologous to mouse POSH (Tapon et al., EMBO J 17:1395-1404 (1998)), with 33 % amino acid identity and 49 % amino acid similarity over the length of the two proteins. Applicant argues that Tapon et al. teaches that POSH has been shown to participate specifically in the activation of the JNK pathway, leading to activation of gene expression in response to PDGF stimulation in COS cells. Full-length POSH protein was found to activate the JNK cascade, but had no effect on actin reorganization.

Applicants also contend that it was well established, before the application was filed, that one can use an oncogene or tumor suppresser gene in cancer diagnosis, prognosis, and in the development of therapeutics and treatment and the nucleotide sequences of these genes can be used (1) as a reference to compare to gene sequences from patients or healthy individuals for mutation analysis, cancer diagnosis and prognosis, (2) as substrates on microarrays for expression analysis in cancer patients, (3) as antisense inhibitors of the over-expressed genes in patients, (4) to produce proteins, antibodies or fusion proteins useful for the diagnosis and development of therapeutics as well. In addition, Applicant asserts that the nucleic acid

sequences can be used to develop primers and probes, the primers can be used in PCR amplification of fragments of the gene, while the probes can be used for expression analysis.

Applicants also argue that some uses can be immediately inferred from a recital of certain properties, as indicated in In re Folkers, 344 F.2d 970, 974 (C.C.P.A. 1965) (explicitly undisturbed by Brenner v. Manson, 383 U.S. 519, 535 n.23 (1966) and In re Kirk, 376 F.2d 936, 949 (C.C.P.A. 1967) (Rich, J., dissenting) "newly discovered compounds [that] belong to a class of compounds, the members of which have become well recognized as useful for a particular purpose because of a particular property, the only reasonable conclusion is that the new compounds, also possessing that property, are similarly useful." Folkers at 975, see also MPEP 2107.02.

Applicants submit because the claimed nucleic acid sequences of the instant application encode a POSH like protein the claimed nucleotide sequences of the instant application belong to a class of compounds, the members of which have well-established utility, the claimed nucleotide sequences which are also capable of these particular purposes, are similarly useful. According to the Federal Circuit, "[t]he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." Juicy F/21, Inc. v. Orange Bang, Inc., 185 F.3d 1364, 1366 (Fed. Cir. 1999) (emphasis added). (See pages 23-26 of the response filed 2/28/05).

In response, Applicants arguments have been fully considered, but are not persuasive.

It is acknowledged that the SEQ ID NO: 3, identified as POSH like protein-1 (POSHL1) has 33% identity and 49% similarity to the amino acid sequence of the POSH protein Taught by Tapon et al. It is also acknowledged that Tapon et al. teaches a polypeptide identified as POSH which is involved in the JNK signal transduction pathway.

However, the instant application has not identified any specific function for the polypeptide(s) of the instant invention (POSHL1) and relies on the alleged function and utility of the POSH polypeptide taught by Tapon et al. for an alleged patentable utility for POSHL1 polypeptide(s). The Applicants assert that the POSHL1 polypeptide(s) have the same function and utility as POSH based solely on sequence similarity. It is respectfully pointed out, however, that the POSHL1 is only 33% identical and 49% similar to the amino acid sequence of POSH (see above). Therefore, there is a high degree of variability between the claimed POSHL1 polypeptide(s) and the POSH polypeptide. It is noted that it would have been well known in the art that sequence similarity does not reliably correlate to structural similarity and that structural similarity does not reliably result in similar or identical biological activities. For example, it would have been well known that even a single nucleotide or amino acid change or mutation can destroy the function of a biomolecule in many instances, albeit not in all cases. Several publications document the unpredictability of the relationship between sequence, structure, and function, although it is acknowledged that certain specific sequences have been found to be conserved in biomolecules having related function following a significant amount of further research. See Attwood (Science, 290:471-473, 2000); Russell et al. (Journal of Molecular Biology, 244:332-350, 1994).

Therefore, it is clear that a polypeptide (POSHL1) that has 33% identity and 49% similarity to a known protein (POSH) does not necessarily have the same and may completely different functions. Therefore, the disclosure that POSHL1 is 33% identical and 49% similar to POSH is not sufficient to establish that POSHL1 and POSH are functionally identical.

With respect to the asserted utilities for the POSH polypeptide taught by Tapon, it is respectfully pointed out that the instant claims are not drawn to POSH, but are drawn to POSHL1 sequences. Nevertheless, the alleged utilities of the POSH sequences as asserted in Applicants response filed 2/28/05 (e.g., cancer diagnosis, prognosis, substrates on microarrays, antisense inhibitors of over-expressed genes, to produce proteins, antibodies or fusion proteins, primers and probes, etc.) are not considered specific and substantial utilities as the asserted utilities for POSH (Tapon et al.) are not specific for POSH but are general utilities which could be a use for any polypeptide or nucleic acid sequence. Therefore, the alleged utility of POSH is not specific and substantial. As such, POSHL1 has not been established as belonging to a class of compounds which have become well recognized as useful for a particular purpose because of a particular property (as required by In re Folkers).

Therefore, the alleged utility of POSH is not sufficient to establish a patentable (i.e., specific and substantial utility for POSHL1), and the rejection is proper.

Conclusion

No claim is allowed

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Mon-Fri, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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